Office Action Summary	Application No.	Applicant(s)	
	10/580,989	ONO ET AL.	
	Examiner	Art Unit	
	DANIEL KOLKER	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 9-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 9-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 May 2006* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/29/07,7/16/07,1/24/08*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *20091002* .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks and amendments filed 29 June 2009 have been entered. Claims 1-4 and 9-15 are pending and under examination.

Election/Restrictions

2. Applicant's election without traverse of Group I (claims 1-4 and 9-15) in the reply filed on 29 June 2009 is acknowledged.

Priority

3. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

4. The information disclosure statements have been considered. A copy of the reference by Kruger, cited on the IDS filed 29 March 2007, was not provided. However as a courtesy to applicant, the examiner has obtained a copy of the reference and has placed it in the case file. The reference has been considered and will appear on the face of any patent that may issue from this application.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 and 9-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to nucleic acids, and methods of using same, wherein the nucleic acids hybridize to certain recited nucleic acids under "stringent conditions". The term "stringent conditions", recited in each of independent claims 1, 3, 9, and 12 is a relative term which renders the claim indefinite. The term "stringent conditions" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear whether low, medium, or high stringency conditions are encompassed by the claims.

Nucleic acids which hybridize under low stringency conditions would not be expected to hybridize under high stringency conditions. Additionally, what constitutes stringent conditions can vary from one person to another. That is, even if the claims were amended to recite a degree of stringency such as “high stringency conditions”, the claims would still be considered indefinite, since it is unclear what constitutes high stringency conditions. While certain stringent conditions are discussed beginning at p. 14 line 20 of the specification, these are exemplary and not limiting. In the absence of reciting specific conditions for hybridization and washes within the claims, one of skill in the art could not determine what nucleic acids are included or excluded by the present claims.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 and 9-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to products comprising nucleic acids which hybridize to a gene, methods using same, and methods of using antibodies that bind to products of a gene. Applicant has also not described the complete genus of nucleic acids that hybridize to a gene, or genes in general, or antibodies that bind to proteins produced by a gene. The claims are akin to example 7 of the Written Description Guidelines Training Materials, available on the USPTO'S web site at http://www.uspto.gov/web/menu/written.pdf, directed to the recitation of allelic variants of genes. The claims are drawn to genera of nucleic acid sequences, including those with regulatory elements, untranslated regions, allelic variants, mutation sequences, and sequences across species as encompassed by the term “gene”. The art teaches that genes have many untranslated regions, and that the interactions of untranslated regions of genes is complex and gene-specific (see Mazumder et al., 2003. Trends in Biochemical Sciences 28:91-98, particularly the paragraph that spans pp. 91 - 92). One of skill in the art would not be able to

know, based on the disclosure, which structural features are necessary for the genes recited in the present claims.

In order to overcome this rejection, it is suggested that applicant amend all claims so that they recite “nucleic acid encoding” rather than “gene encoding”. Similarly, claims which recite “translation products of one or more genes” should be amended to recite “proteins encoded by nucleic acids", or similar language.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Millonig 2000 (Nature 403:764-769,cited on IDS filed 29 March 2007), as evidenced by Genbank accession AF226662.

Millonig teaches cloning mouse Lmx1a-encoding nucleic acid. Partial sequence information is given at Figure 3, and detailed methods of the cloning procedure are set forth at p. 768, the section spanning the two columns. The reference also teaches that the sequence information was submitted to GenBank and given the accession number AF226662 (p. 769, top, in the Acknowledgements section). The sequence alignment below shows that AF226662 encodes present SEQ ID NO:14. Note that the alignment shows that 100% of the residues are aligned perfectly. As the prior art product is 100% identical to a nucleic acid encoding SEQ ID NO:14 and as it is over 15 nucleotides, it anticipates claims 3-4.

```
RESULT 1
AF226662
LOCUS       AF226662               1149 bp    mRNA    linear   ROD 13-MAR-2000
DEFINITION  Mus musculus lim homeodomain-containing transcription factor
            (Lmx1a) mRNA, complete cds.
ACCESSION   AF226662
VERSION     AF226662.1  GI:7230570
KEYWORDS    .
SOURCE      Mus musculus (house mouse)
  ORGANISM  Mus musculus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
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            Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia;
            Sciurognathi; Muroidea; Muridae; Murinae; Mus.
REFERENCE   1  (bases 1 to 1149)
  AUTHORS   Millonig,J.H., Millen,K.J. and Hatten,M.E.
  TITLE     The mouse Dreher gene Lmx1a controls formation of the roof plate
in the vertebrate CNS
  JOURNAL   Nature 403 (6771), 764-769 (2000)
   PUBMED   10693804
REFERENCE   2  (bases 1 to 1149)
  AUTHORS   Millen,K.J., Millonig,J.H. and Hatten,M.E.
  TITLE     Direct Submission
  JOURNAL   Submitted (17-JAN-2000) Laboratory of Developmental Neurobiology,
            The Rockefeller University, Box 109, 1230 York Avenue, New York,
NY
            10021, USA
FEATURES             Location/Qualifiers
     source          1. .1149
                     /organism="Mus musculus"
                     /mol_type="mRNA"
                     /strain="C3HeB/Fele-a/a"
                     /db_xref="taxon:10090"
                     /chromosome="1"
                     /map="88.6"
     gene            1. .1149
                     /gene="Lmx1a"
     CDS             1. .1149
                     /gene="Lmx1a"
                     /function="required for roof plate formation in the
                     vertebrate CNS"
                     /note="mutated in the sponataneous mouse neurological
                     mutant, dreher"
                     /codon_start=1
                     /product="lim homeodomain-containing transcription
factor"
                     /protein_id="AAF43012.1"
                     /db_xref="GI:7230571"

/translation="MLDGLKMEENFQSAIETSASFSSLLGRAVSPKSVCEGCQRVISD

RFLLRLNDSFWHEQCVQCASCKEPLETTCFYRDKKLYCKYHYEKLFAVKCGGCFEAIA

PNEFVMRAQKSVYHLSCFCCCVCERQLQKGDEFVLKEGQLLCKGDYEKERELLSLVSP

AASDSGKSDDEESLCKSAHGAGKGASEDGKDHKRPKRPRTILTTQQRRAFKASFEVSS

KPCRKVRETLAAETGLSVRVVQVWFQNQRAKMKKLARRQQQQQQDQQNTQRLTSAQTN

GSGNAGMEGIMNPYTTLPTPQQLLAIEQSVYNSDPFRQGLTPPQMPGDHMHPYGAEPL
                     FHDLDSDDTSLSNLGDCFLATSEAGPLQSRVGNPIDHLYSMQNSYFTS"
     misc_feature    121. .264
                     /gene="Lmx1a"
                     /note="Region: lim1 Zn-finger domain"
     misc_feature    277. .450
                     /gene="Lmx1a"
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                     /note="Region: lim2 Zn-finger domain"
     misc_feature    580. .762
                     /gene="Lmx1a"
                     /note="Region: DNA-binding domain"
ORIGIN

Alignment Scores:
Length:                 1149
Score:                  2031.00        Matches:       382
Percent Similarity:     100.0%         Conservative:  0
Best Local Similarity:  100.0%         Mismatches:    0
Query Match:            100.0%         Indels:        0
DB:                     14             Gaps:          0

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Qy          1 MetLeuAspGlyLeuLysMetGluGluAsnPheGlnSerAlaIleGluThrSerAlaSer 20
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 ATGTTGGACGGCCTGAAGATGGAGGAGAACTTTCAAAGTGCGATTGAGACCTCGGCATCT 60

Qy         21 PheSerSerLeuLeuGlyArgAlaValSerProLysSerValCysGluGlyCysGlnArg 40
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TTCTCCTCTTTGCTGGGCAGAGCGGTGAGCCCCAAGTCTGTCTGCGAGGGCTGTCAGCGG 120

Qy         41 ValIleSerAspArgPheLeuLeuArgLeuAsnAspSerPheTrpHisGluGlnCysVal 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GTCATCTCGGACAGGTTTCTGCTGCGGCTCAACGACAGCTTCTGGCACGAGCAATGCGTG 180

Qy         61 GlnCysAlaSerCysLysGluProLeuGluThrThrCysPheTyrArgAspLysLysLeu 80
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 CAGTGTGCCTCCTGCAAAGAGCCCCTGGAGACCACCTGCTTCTACCGGGACAAGAAGCTC 240

Qy         81 TyrCysLysTyrHisTyrGluLysLeuPheAlaValLysCysGlyGlyCysPheGluAla 100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 TACTGCAAGTACCACTACGAGAAACTGTTTGCTGTCAAATGTGGGGGCTGCTTCGAGGCC 300

Qy        101 IleAlaProAsnGluPheValMetArgAlaGlnLysSerValTyrHisLeuSerCysPhe 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 ATTGCGCCCAATGAGTTTGTCATGCGTGCCCAGAAGAGCGTATACCACCTGAGCTGCTTC 360

Qy        121 CysCysCysValCysGluArgGlnLeuGlnLysGlyAspGluPheValLeuLysGluGly 140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 TGCTGCTGCGTCTGTGAGCGACAGCTGCAGAAGGGTGACGAGTTTGTCCTGAAGGAGGGC 420

Qy        141 GlnLeuLeuCysLysGlyAspTyrGluLysGluArgGluLeuLeuSerLeuValSerPro 160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 CAGCTGCTCTGCAAAGGGGACTATGAGAAAGAACGGGAGCTGCTGAGCCTGGTGAGCCCT 480

Qy        161 AlaAlaSerAspSerGlyLysSerAspAspGluGluSerLeuCysLysSerAlaHisGly 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 GCGGCCTCAGACTCAGGCAAAAGCGATGATGAGGAGAGCCTTTGCAAGTCAGCCCATGGG 540

Qy        181 AlaGlyLysGlyAlaSerGluAspGlyLysAspHisLysArgProLysArgProArgThr 200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db        541 GCAGGAAAAGGAGCATCAGAGGACGGCAAGGACCATAAGCGACCCAAACGTCCCAGAACT 600

Qy        201 IleLeuThrThrGlnGlnArgArgAlaPheLysAlaSerPheGluValSerSerLysPro 220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 ATCCTGACCACTCAGCAGAGGAGAGCATTCAAGGCCTCGTTTGAAGTATCCTCCAAGCCC 660

Qy        221 CysArgLysValArgGluThrLeuAlaAlaGluThrGlyLeuSerValArgValValGln 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 TGCAGAAAGGTGAGGGAGACTCTGGCTGCGGAGACAGGGCTGAGTGTCCGTGTGGTTCAG 720

Qy        241 ValTrpPheGlnAsnGlnArgAlaLysMetLysLysLeuAlaArgArgGlnGlnGlnGln 260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 GTGTGGTTCCAGAACCAGCGAGCCAAGATGAAGAAGCTGGCCCGGCGACAGCAGCAACAG 780

Qy        261 GlnGlnAspGlnGlnAsnThrGlnArgLeuThrSerAlaGlnThrAsnGlySerGlyAsn 280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 CAACAGGACCAACAGAACACCCAGAGGCTGACTTCTGCTCAGACAAATGGTAGTGGGAAT 840

Qy        281 AlaGlyMetGluGlyIleMetAsnProTyrThrThrLeuProThrProGlnGlnLeuLeu 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 GCGGGCATGGAAGGGATCATGAACCCCTATACAACGTTGCCCACCCCACAGCAGCTGCTG 900

Qy        301 AlaIleGluGlnSerValTyrAsnSerAspProPheArgGlnGlyLeuThrProProGln 320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 GCCATTGAACAGAGCGTCTACAACTCTGATCCCTTCCGACAGGGTCTCACCCCACCCCAG 960

Qy        321 MetProGlyAspHisMetHisProTyrGlyAlaGluProLeuPheHisAspLeuAspSer 340
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 ATGCCTGGAGATCACATGCACCCCTATGGTGCTGAACCTCTTTTCCATGACTTGGATAGT 1020

Qy        341 AspAspThrSerLeuSerAsnLeuGlyAspCysPheLeuAlaThrSerGluAlaGlyPro 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 GATGACACATCTCTCAGTAACCTGGGAGACTGCTTCCTGGCAACCTCAGAAGCTGGGCCC 1080

Qy        361 LeuGlnSerArgValGlyAsnProIleAspHisLeuTyrSerMetGlnAsnSerTyrPhe 380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 CTGCAGTCCAGAGTGGGAAACCCCATTGACCATCTGTACTCCATGCAGAATTCCTATTTC 1140

Qy        381 ThrSer 382
              ||||||
Db       1141 ACCTCT 1146
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Note that the nucleic acids encoding SEQ ID NO:14, 16, and 18 are admitted prior art; see p. 11 lines 21-33 and p. 12 final paragraph in the specification.

8. Claims 1-4, 9, and 13-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Smidt 2000 (Nature Neuroscience 3:337-341).

Smidt teaches nucleic acids encoding Lmx1b, as well as methods of using same. The nucleic acid is a fragment of rat Lmx1b, and encodes an amino acid that is 100% identical to the

amino acids encoded by mouse Lmx1b with GenBank accession number AF078166; see p. 337 second column first paragraph. The nucleic acid used by Smidt was 115 bp long, as encompassed by claims 1-4. Although the nucleic acids identified by SEQ ID NO: in independent claims 1, 3, and 9 are not identical to those disclosed by Smidt, the claims do not require identity. The claims are considerably broader, in that they are drawn to "a polynucleotide that hybridizes under stringent conditions to a transcript of a gene that consists of a nucleotide sequence" listed within the claims. The alignment shown below provides evidence that AF078166, i.e. the nucleic acid encoded by Smidt's cDNA, will hybridize to a nucleic acid encoding instant SEQ ID NO:14. In the alignment, the top line is the amino acid sequence SEQ ID NO:14, and the bottom line is AF078166. Given the long stretches of identity across the entirety of the sequences, the nucleic acids from Smidt will inherently hybridize to nucleic acids encoding SEQ ID NO:14.

```
RESULT 1
AF078166
; Sequence AF078166, Application AF078166
; GENERAL INFORMATION:
;  APPLICANT:
;  APPLICANT:
;  APPLICANT:
;  TITLE OF INVENTION:
;  FILE REFERENCE:
;  CURRENT APPLICATION NUMBER:
;  CURRENT FILING DATE:
;  PRIOR APPLICATION NUMBER:
;  PRIOR FILING DATE:
;  PRIOR APPLICATION NUMBER:
;  PRIOR FILING DATE:
;  NUMBER OF SEQ ID NOS:
;  SOFTWARE:
; SEQ ID NO AF078166
;   LENGTH:
;   TYPE: DNA
;   ORGANISM:
AF078166

Alignment Scores:
Pred. No.:              0              Length:         1119
Score:                  82.50          Matches:        190
Percent Similarity:     65.4%          Conservative:   43
Best Local Similarity:  53.4%          Mismatches:     120
Query Match:            52.4%          Indels:         3
DB:                     3              Gaps:           1

US-10-580-989-14 (1-382) x AF078166 (1-1119)
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```
Qy         19 AlaSerPheSerSerLeuLeuGlyArgAlaValSerProLysSerValCysGluGlyCys 38
              |||      :::::::::::::::::::::::            |||||||||||||||
Db         49 GCCACCCTGGGGGTGCTGCTGGGCTCCGACTGCCCGCATCCCGCCGTCTGCGAGGGCTGC 108

Qy         39 GlnArgValIleSerAspArgPheLeuLeuArgLeuAsnAspSerPheTrpHisGluGln 58
              ||||||   ||||||||||||||||||   |||   |||   |||   |||||||||
Db        109 CAGCGGCCCATCTCCGACCGCTTCCTGATGCGAGTCAACGAGTCGTCCTGGCACGAGGAG 168

Qy         59 CysValGlnCysAlaSerCysLysGluProLeuGluThrThrCysPheTyrArgAspLys 78
              |||   |||||||||   |||         |||   |||   |||      |||||:::
Db        169 TGTTTGCAGTGCGCGGCATGTCAGCAAGCCCTCACCACCAGCTGCTACTTCCGGGATCGG 228

Qy         79 LysLeuTyrCysLysTyrHisTyrGluLysLeuPheAlaValLysCysGlyGlyCysPhe 98
              ||||||||||||||   :::|||      |||||||||:::|||||||:::|||||||
Db        229 AAACTGTACTGCAAACAAGACTACCAACAGCTCTTCGCGGCAAAGTGCAGCGGCTGCATG 288

Qy         99 GluAlaIleAlaProAsnGluPheValMetArgAlaGlnLysSerValTyrHisLeuSer 118
              |||   |||||||||   ||||||||||||||||||      :::|||||||||||||:::
Db        289 GAGAAGATCGCGCCTACCGAGTTCGTCATGCGGGCGCTGGAGTGTGTGTACCACTTGGGC 348

Qy        119 CysPheCysCysCysValCysGluArgGlnLeuGlnLysGlyAspGluPheValLeuLys 138
              ||||||||||||||||||||||||||||||||   |||||||||||||||||||||||||
Db        349 TGTTTCTGCTGCTGTGTGTGCGAGAGGCAACTGCGCAAGGGGGACGAGTTCGTGCTCAAG 408

Qy        139 GluGlyGlnLeuLeuCysLysGlyAspTyrGluLysGluArgGluLeuLeuSerLeuVal 158
              |||||||||||||||||||||||||||||||||||:::   |||||||||   |||
Db        409 GAGGGCCAGCTGCTGTGCAAGGGTGACTATGAGAAGGAGAAAGACCTGCTCAGCTCCGTG 468

Qy        159 SerProAlaAlaSerAspSerGlyLysSerAspAspGluGluSerLeuCysLysSerAla 178
              ||||||:::   |||||||||:::|||||||   ||||||   :::   :::|||   |||
Db        469 AGCCCGGACGAGTCTGACTCTGTGAAGAGTGAGGATGAAGATGGAGACATGAAGCCGGCC 528

Qy        179 HisGlyAlaGly---------LysGlyAlaSerGluAspGlyLysAspHisLysArgPro 195
              :::|||   |||         ||||||   :::   ||||||||||||   :::||||||
Db        529 AAGGGGCAGGGCAGCCAGAGTAAAGGCAGTGGAGATGACGGGAAAGACCCGAGAAGGCCC 588

Qy        196 LysArgProArgThrIleLeuThrThrGlnGlnArgArgAlaPheLysAlaSerPheGlu 215
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        589 AAACGGCCCCGAACCATCCTCACCACACAGCAGCGAAGAGCTTTCAAGGCATCCTTTGAG 648

Qy        216 ValSerSerLysProCysArgLysValArgGluThrLeuAlaAlaGluThrGlyLeuSer 235
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        649 GTCTCCTCCAAGCCCTGTCGGAAGGTCCGAGAGACATTGGCAGCAGAGACAGGCCTCAGC 708

Qy        236 ValArgValValGlnValTrpPheGlnAsnGlnArgAlaLysMetLysLysLeuAlaArg 255
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        709 GTGCGTGTGGTCCAGGTCTGGTTTCAGAACCAAAGAGCAAAGATGAAGAAGCTGGCCCGG 768

Qy        256 ArgGlnGlnGlnGlnGlnGlnAspGlnGlnAsnThrGlnArgLeuThrSerAlaGlnThr 275
              |||   ||||||||||||      |||                        :::
Db        769 AGACACCAGCAACAGCAGGAGCAGCAGAACTCCCAGCGGCTGGGCCAAGAGGTTCTGTCA 828

Qy        276 AsnGlySerGlyAsnAlaGlyMetGluGlyIleMetAsnProTyrThrThrLeuProThr 295
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                ::::::      :::   :::          :::
Db        829 AGCCGCATGGAGGGCATGATGGCCTCCTACACCGCGCTGGCCCCTCCGCAGCAGCAGATC 888

Qy        296 ProGlnGlnLeuLeuAlaIleGluGlnSerValTyrAsnSerAspProPheArgGlnGly 315
                                       |||::::::
Db        889 GTGGCCATGGAGCAGAGCCCCTACGGAAGCAGCGACCCCTTCCAACAGGGCCTCACGCCG 948

Qy        316 LeuThrProProGlnMetProGlyAspHisMetHisProTyrGlyAlaGluProLeuPhe 335
                    |||         :::      ::::::   :::::::::      |||
Db        949 CCCCAAATGCCAGGGAACGACTCCATCTTCCACGATATTGATAGTGATACCTCCCTCACC 1008

Qy        336 HisAspLeuAspSerAspAspThrSerLeuSerAsnLeuGlyAspCysPheLeuAlaThr 355
              :::      |||:::          |||   :::      :::             :::
Db       1009 AGCCTCAGCGACTGCTTCCTCGGCTCTTCCGACGTGGGCTCCCTGCAGGCGCGCGTGGGG 1068

Qy        356 SerGluAlaGlyProLeuGlnSerArgValGlyAsnProIleAspHis 371
                    :::   |||   |||:::   :::         ::::::
Db       1069 AACCCCATTGACCGGCTCTACTCCATGCAGAGCTCCTACTTTGCCTCC 1116
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Smidt also teaches methods of using the Lmx1b cDNA to detect dopaminergic neurons. Specifically, at p. 337 final paragraph the reference teaches that nucleic acid encoding Lmx1b was used to detect these neurons; see also Figures 1-2. The reference teaches every step of claim 1, as well as the starting materials encompassed by claims 1-4. Furthermore, Smidt teaches the step of contacting the cellular samples with antibodies that bind to Ptx3 (see Figure 2d), anticipating claim 9. Claim 13 is anticipated as the probe from Smidt is more than 15 nucleotides long. Claim 14 is anticipated as Smidt teaches in situ hybridization assays to detect both the reagent of claim 3 (which is sufficiently broad to include Lmx1b-encoding nucleic acids) and TH. Claim 15 is anticipated as the reference teaches both the reagent of claim 3 (which is sufficiently broad to include Lmx1b-encoding nucleic acids) and antibodies against Ptx3, as shown in Figure 2d. Although the Smidt reference does not refer to the two products as "a kit", the reference nonetheless anticipates claims 14-15 since it teaches all elements of the claimed kits together.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 9-10, and 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smidt 2000 (Nature Neuroscience 3:337-341) in view of Holzschuh 2001 (Mechanisms of Development 101:237-243).

The reasons why claims 1-4, 9, and 13-15 are anticipated by Smidt are set forth above. Briefly, the reference teaches contacting a cellular sample with a nucleic acid that will hybridize to one or more of the nucleic acids listed in the claims to detect dopaminergic neurons, and also teaches detecting Ptx3 to confirm that a dopaminergic neuron is present. However Smidt does not teach detecting DAT as recited in claim 10 and 12.

Holzschuh teaches that DAT (dopamine transporter) is expressed in dopaminergic neurons, and that this marker can be used to distinguish truly dopaminergic cells from other catecholamine-containing cells. However Holzschuh does not teach the method of claims 1 or 9 or the product of claim 3.

It would have been obvious to one of ordinary skill in the art to modify the methods set forth by Smidt to include the steps taught by Holzschuh, thereby arriving at the invention recited in claims 10 and 12. Doing so would have been advantageous, Holzschuh teaches that DAT is particularly useful to identify dopaminergic neurons.

Allowable Subject Matter

10. The prior art indicates that LMX1A is expressed in the brain (see for example Millonig et al. (2000), Nature 403:764-769, cited on IDS filed 29 March 2007). However the prior art does not teach or suggest that LMX1A protein (SEQ ID NO:14, 16, or 18) or nucleic acid (SEQ ID NO: 13, 15, 17) is expressed in ventral midbrain in particular or that it is expressed in dopaminergic neurons.

In order to expedite prosecution the examiner recommends the following amendments:

A) Rewrite claim 1 as follows:

A method for detecting or selecting a dopaminergic neuron and/or a progenitor cell thereof, wherein the method comprises the step of contacting a cellular sample with a polynucleotide comprising:

(1) the nucleotide sequence of SEQ ID NO:13;

(2) a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:14;

(3) the nucleotide sequence of SEQ ID NO:15 or 17; or

(4) a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:15 or 16;

wherein the cellular sample comprises cells from the ventral midbrain of an animal.

B) Rewrite claim 9 as follows:

A method for detecting or selecting a dopaminergic neuron and/or a progenitor cell thereof, wherein the method comprises the steps of:

(a) contacting a cellular sample that comprises cells from the ventral midbrain of an animal with a polynucleotide comprising:

(1) the nucleotide sequence of SEQ ID NO:13;

(2) a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:14;

(3) the nucleotide sequence of SEQ ID NO:15 or 17; or

(4) a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:15 or 16; and

(b) contacting the cellular sample with a polynucleotide that encodes one or more proteins, or with an antibody that binds to one or more proteins, wherein the one more proteins is selected from the group consisting of Lmx1b, Nurr1, En1, Ptx3, and TH.

C) Rewrite claim 10 as follows:

The method of claim 9, which further comprises the step of:

(c) contacting the cellular sample with a polynucleotide that encodes one or more proteins, or with an antibody that binds to one or more proteins, wherein the one or more proteins is selected from the group consisting of DAT and ADH2.

D) Rewrite claim 11 as follows:

The method of claim 9, wherein the one or more proteins in step (b) is selected from the group consisting of Lmx1b, Nurr1, and En1.

E) Rewrite claim 12 as follows:

A method for detecting or selecting a dopaminergic neuron and/or a progenitor cell thereof, wherein the method comprises the steps of:

(a) contacting a cellular sample that comprises cells from the ventral midbrain of an animal with a polynucleotide comprising:

(1) the nucleotide sequence of SEQ ID NO:13;

(2) a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:14;

(3) the nucleotide sequence of SEQ ID NO:15 or 17; or

(4) a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:15 or 16; and

(b) contacting the cellular sample with a polynucleotide that encodes one or more proteins, or with an antibody that binds to one or more proteins, wherein the one or more proteins is selected from the group consisting of DAT and ADH2.

F) Cancel claims 2-4 and 13-15.

Support for the amendment from “consisting of” to “comprising can be found in original claims 1, 9, and 12 (drawn to methods of using nucleic acids which hybridize to recited nucleic acids; although the recited nucleic acids use “consisting of” language, nucleic acids which comprise same would hybridize) and original claim 3, drawn to reagents comprising a nucleic acid that hybridizes to recited sequences. Support for the amendment limiting the methods to contacting cells from the ventral midbrain of an animal can be found in the specification at p. 31 final paragraph, p. 36 line 34 - p. 37 line 3, and p. 40 lines 1-3.

Conclusion

11. No claim is allowed.

12. The art made of record and not relied upon is considered pertinent to applicant's disclosure:

Perlmann U.S. Patent Application Publication 2008/0311091, published 18 December 2008, PCT filed 22 December 2005, claiming benefit of a provisional application filed 23 December 2004. The references discloses that Lmx1a, when expressed in embryonic stem cells, directs them to a dopaminergic fate (see for example paragraph [0009] and claim 86). However the reference does not constitute prior art as the earliest effective filing date (23 December 2004, the date the provisional application was filed) is after the date that the present application was filed in this country (the date of filing of PCT/JP04/17574 is the date that it was effectively filed in this country).

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANIEL KOLKER whose telephone number is (571)272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel E. Kolker/
Primary Examiner, Art Unit 1649
October 8, 2009